REMARKS

Claims 1-2, 4-5, 7-13, 15-20, 22, 24-31 and 33 are currently pending.

I. Outstanding Objection and Rejections

Claim 16 is subject to objection for failing to indicate the nature of the amendment to that claim in Applicant's amendment of September 1, 2005. Claims 1-31 and 33 stand rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Pat. No. 6,379 674 B1 issued to Rabkin et al. (hereinafter, "Rabkin"). In addition, claims 1, 5, 19, and 22 are rejected under 35 U.S.C. § 103(a) over Rabkin in view of U.S. Pat. No. 5,328,688 (hereinafter, "Roizman '688"). Claims 1, 7-8, 12-13, 15-16, 18-19, 25-26, and 30 were rejected under § 103(a) over Rabkin in view of Andreansky et al., Gene Ther. 5:121-130 (1998) (hereinafter, "Andreansky"). Finally, claims 1, 9-11, 19, and 27-29 were rejected under § 103(a) over Rabkin in view of U.S. Pat. No. 5,641,651 (hereinafter, "Roizman '652").

II. Patentability Arguments

A. The objection to claim 16

The Examiner objected to claim 16 because it recited an "EGF-1" promoter in the amendment dated September 1, 2005, but did not contain markings to indicate that the claim was being changed to recite an "EGF-1 promoter" rather than the "EGR-1 promoter" recited in original claim 16. The Examiner noted that a typographical error appeared to be responsible for the change in the language of claim 16. Applicant thanks the Examiner for identifying the altered language of claim 16 and confirms that the alteration arose through a typographical error. To eliminate all doubt and any possibility for confusion, Applicant has canceled claim 16 and added new claim 34, which contains language identical to the language of original claim 16. The amendment does not alter the scope of the subject matter of original claim 16 and was not made in response to any patentability concern raised by the Examiner.

B. The rejection under 35 U.S.C. § 102(e) over Rabkin

In the Office Action mailed November 1, 2005 at pages 3-5, the Examiner rejected claims 1-2, 4, 17, 19-20, 24, 31 and 33 as anticipated by Rabkin. In support, the Examiner stated that Rabkin disclosed mutated HSV that are incapable of expressing a functional $\gamma_1$34.5 gene product, such as the G207 HSV mutant, and which comprise at least one expressible nucleotide sequence encoding an immunomodulator such as GM-CSF.

Applicant notes that Rabkin, at page 11, lines 26-30, provides a list of immunomodulators, including without distinction IL-4, GM-CSF, and others, the genes for which would be suitable for inclusion in the mutated HSV.

Applicant attaches to this document, as Appendix 1, a declaration under 37 C.F.R. § 1.131 by Richard J. Whitley, M.D. (hereinafter, the "Whitley declaration"), a named inventor on the above-captioned application. The Whitley declaration includes an Exhibit A containing copies of laboratory notebook pages, with dates redacted, and an Exhibit B that contains a copy of the declarant's curriculum vitae. In the declaration, Dr. Whitley establishes the construction of a plurality of herpes simplex virus vectors according to the claims at a time prior to August 12, 1997, the earliest effective filing date for Rabkin. In particular, Dr. Whitley discloses the construction of R8306, a mutant HSV containing a deletion in each $\gamma_1$34.5 gene and encoding murine interleukin-4, an immunomodulatory cytokine. Dr. Whitley also discloses the construction of R8308, a mutant HSV containing a deletion in each $\gamma_1$34.5 gene and encoding murine interleukin-10. Each of these HSV constructs is supported by the laboratory notebook pages attached to the Whitley declaration.

Further, the Whitley declaration establishes that each of these HSV viral vector constructs was able to productively infect human tumorigenic cells, i.e., U251MG and D54MG human glioma cells. The titers measured during infection of these cells revealed that the titers of each of R8306 and R8308 increased with increasing time post-infection, consistent with a productive infection.

In addition, the Whitley declaration, corroborated by laboratory notebook pages attached thereto, establishes that each of the mutant HSV vectors, R8306 and R8308, was injected into mice harboring human glioma cells and survival curves demonstrated that each viral vector prolonged the survival of the injected mice.

For the foregoing reasons, Applicant submits that the inventors were in possession of $\gamma_1$34.5 double mutant HSV vectors comprising a coding region for an immunomodulatory cytokine, such as IL-4. That subject matter was in the possession of the inventors, moreover, at a point in time prior to August 12, 1997, the earliest effective filing date that could be accorded to Rabkin. As noted, Rabkin, assertedly discloses a $\gamma_1$34.5

double mutant HSV vector comprising a coding region for an immunomodulatory cytokine selected from a list of cytokines including IL-4, GM-CSF, and others. Accordingly, Rabkin is not available as art citable under 35 U.S.C. § 102(e) against the pending claims. See M.P.E.P. § 715.02. Therefore, the rejection of claims 1-2, 4, 17, 19-20, 24, 31 and 33 under § 102(e) as anticipated by Rabkin has been overcome and should be withdrawn.

C. Obviousness Rejections

1. The rejections over Rabkin in view of various secondary references

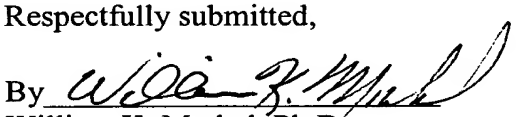
The Examiner rejected various claims as obvious under 35 U.S.C. § 103(a) over Rabkin as a primary reference in view of a variety of secondary references (Roizman '688, Andreansky, and Roizman '651). As established above, the Whitley declaration attached hereto effectively removes Rabkin as a prior art reference available against the pending claims under 35 U.S.C. § 102(e). None of the secondary references, Roizman '688, Andreansky or Roizman '651, can remedy the deficiencies created by the removal of Rabkin. Accordingly, each one of the rejections of various claims under 35 U.S.C. § 103(a) over Rabkin in view of any of Roizman '688, Andreansky, or Roizman '651 has been overcome and each of these rejections should be withdrawn.

Conclusion

In view of the above amendments and remarks, Applicant submits that the objection and each of the outstanding rejections of the claims has been overcome and claims 1-2, 4-5, 7-13, 15, 17-20, 22, 24-31, and 33-34 are now in condition for allowance.

Dated: March 1, 2006

Respectfully submitted,

By 

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APPENDIX 1